

AMENDMENTS TO SPECIFICATION

[0017] Fig. 2 is a graphical representation of the results obtained in experiments to study the effects of PAI- 1 on the vasoactivity of tPA. The EC50 of PE was determined in the absence (Control) or presence of 1 nM tPA, 20 nM tPA, 1 nM tPA and an equimolar concentration of PAI-1, 20 nM tPA and an equimolar concentration of PAI-1, 1nM tPA and 2 µM of EEIIMD or 20 nM tPA and 2 µM of [[EEIMD]] EEIIMD.

[0018] Fig.3 is a graphical representation of the results obtained in experiments to study the effect of RAP and anti-LRP antibodies on the vasoactivity of tPA. The EC50 of PE was determined in the absence (Control) or presence of 1 nM tPA, 20nM tPA, 1nM tPA and an equimolar concentration of PAI-1, 20nM tPA and an equimolar concentration of PAI-1, 1 nM tPA and 2µM [[or]] of EEIIMD or 20 nM tPA and 2 µM of [[EEIMD]] EEIIMD.

[0030] The peptide of the present invention, while preventing and/or inhibiting the adverse effects of scuPA on blood vassels, has no such preventive and/or inhibitory effect on the fibrinolytic activity of scuPA. The peptide is therefore useful in clot lysis during thrombolytic therapy in myocardial infarction, stroke and related complications.

[0034] The preferred dosage regimen for the peptide consists of an amount effective to optimally enhance the activity of the fibrinolytic [[activity]] agent while also preventing the harmful vasoactive effects of a fibrinolytic agent on a case by case basis. The peptide

may be a component of a sequence of varying numbers of amino acids, or the peptide may have a modification of one or more amino acids in its sequence. The ratio of peptide/tPA, uPA, or TNK-tPA may be in the range of 0.1/1.0 to 1.0/0.1.

[0055] PAI-1 interacts with tPA through independent sites; the catalytic site and a docking site, present in the amino acids 296 to 299. The PAI-1 docking site is mutated in TNK-tPA. To examine in greater detail the role of the PAI-1 docking site in the vasoactivity of TNK-tPA specifically and of rtPA in general, we examined the effect of the PAI-1 derived hexapeptide [[EEIMD]] EEIIMD that correspond to the amino acid residues 350 to 355 of PAI-1 (the epitope in PAI-1 that interacts with tPA docking site) Madison EL, Goldsmith EJ, Gerard RD, Gethinng MJH, Sambrook JF, Bassel-Duby RS. Amino acid residues that affect interaction of tissue plasminogen activator with tissue plasminogen inhibitor 1. *Proceedings of National Academy of Science, USA* 1990; 87:3530-3534. Madison EL, Goldsmith EJ, Gething M-JH., Sambrook JF, Gerard RD. Restoration of serine protease-inhibitor interaction by protein engineering . *Journal of Biological Chemistry* 1990;265:21423-21426.